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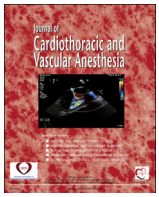

Original Article

Sevoflurane Relieves Lung Function Deterioration After Cardiopulmonary Bypass

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Objective: To investigate sevoflurane's potential to alleviate the detrimental pulmonary changes after cardiopulmonary bypass (CPB).
Design: Prospective, randomized clinical investigation.
Setting: University hospital.
Participants: One hundred ninety patients undergoing elective cardiac surgery.
Interventions: Ninety-nine patients under intravenous anesthesia were administered 1 minimal alveolar concentration of sevoflurane for 5 minutes after being weaned from CPB (group SEV); intravenous anesthesia was maintained in the other 91 patients (group CTRL).
Measurements and Main Results: Measurements were performed with open chest: before CPB, after CPB, and after intervention. The lungs' mechanical impedance and capnogram traces were recorded, arterial and central venous blood samples were analyzed, and lung compliance was documented. Airway resistance, tissue damping, and elastance were obtained from the impedance spectra. The capnogram phase III slope was determined using linear regression. The partial pressure of oxygen in the arterial blood/fraction of inspired oxygen ratio and shunt fraction were calculated from blood gas parameters. After CPB, sevoflurane induced bronchodilation, reflected in marked drops in airway resistance and smaller improvements in lung tissue viscoelasticity indicated by decreases in tissue damping and elastance. These changes were reflected in a decreased capnogram phase III slope and shunt fraction and increased partial pressure of oxygen in the arterial blood/fraction of inspired oxygen ratio and lung compliance. The more severe deteriorations that occurred after CPB, the greater improvements by sevoflurane were observed.
Conclusions: Sevoflurane can alleviate CPB-induced bronchoconstriction, compromised lung tissue mechanics, and enhanced intrapulmonary shunt. This benefit has particular importance in patients with severe CPB-induced lung function deterioration.

Key Words: inhalation anesthesia; extracorporeal circulation; respiratory mechanics; capnography; ventilation; heterogeneity

VOLATILE ANESTHETICS have marked relaxation potential on the airway smooth muscle, resulting in complex pulmonary consequences. Their bronchodilator activity against an elevated bronchial tone caused by exogenous constrictor agonists has been proved consistently in experimental studies.[1–3] Airway dilation by volatile agents also has been confirmed after endogenous release of constrictor mediators in clinical investigations; elevations in the airway tone in these previous clinical studies were induced by administering thiopental and succinylcholine and/or performing endotracheal intubation.[4,5]

Another relevant trigger of perioperative bronchoconstriction is cardiopulmonary bypass (CPB) applied during cardiac surgery.[6,7] The use of this technique induces well-described multimodal detrimental changes in the lungs.[8] The systemic

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inflammatory response is initiated by contact activation, ischemia-reperfusion, and endotoxemia, which are followed by the activation of complement, cytokine, and coagulation/fibrinolysis cascades[9–11] which, in turn, result in leukocyte activation.[12] Free oxygen radicals, platelet-activating factor, and leukotrienes increase vascular permeability and interstitial edema.[13] Furthermore, mast cells and basophils release bronchoactive mediators, such as histamine and serotonin.[14,15] The subsequent overall pulmonary dysfunction can be manifested in important clinical pathologies, such as airway constriction, atelectasis, hypoxemia, elevated right heart afterload, and reduced systemic venous return.

Sevoflurane is among the most commonly used volatile anesthetics, with beneficial pharmacokinetic properties, and advantageous bronchial effects compared with other volatile anesthetics.[4] The effects of sevoflurane on lung function have been investigated extensively in humans and animal models. However, in these studies simple bronchial challenges were applied, mainly inducing specific bronchoconstriction of cholinergic or histaminergic origin.[1,16,17] Even though the beneficial pulmonary profile of sevoflurane after CPB can be anticipated, the only previous study to investigate its effects on the lungs after this complex challenge was limited to demonstrating beneficial changes in leukocyte counts and interleukin levels.[18] Furthermore, the effects of sevoflurane on lung functional changes, particularly increased interstitial edema and ventilation heterogeneity after CPB, have not been investigated. The authors therefore aimed to characterize the therapeutic potential of this volatile agent against adverse pulmonary changes induced by CPB by assessing airway and lung tissue mechanics, ventilation heterogeneity, ventilation-perfusion mismatch, and gas exchange. The authors hypothesized that after deleterious lung function changes from CPB, the expected bronchodilation by sevoflurane is associated with improvements in lung tissue viscoelasticity and diminished ventilation heterogeneities, which may enhance oxygenation.

Methods

Patients

The protocol was approved by the Human Research Ethics Committee, University of Szeged, Hungary (No. WHO 2788). Patients undergoing elective cardiac surgery were enrolled in the study between September 2014 and November 2015; the process is shown in Figure 1. Inclusion criteria were an ejection fraction $>30\%$, a body mass index <35 kg/m^2, and a lack of endocarditis. Written, informed consent was obtained from the patients participating in the study, who then were assigned randomly to the sevoflurane group (SEV) or the control group (CTRL). Measurement data of 190 participants (SEV [n = 99], CTRL [n = 91]; 107 males, 83 females, 63 y of age [range 32-85 y]) were included in the analysis. Table 1 summarizes the demographic, anthropometric, and clinical characteristics of the patients.

Anesthesia and Surgery

The patients were premedicated with intramuscular morphine (0.07 mg/kg) and midazolam (0.07 mg/kg) 1 hour before the surgery. Anesthesia was induced with intravenous (IV) midazolam (30 μg/kg), sufentanil (0.4-0.5 μg/kg), and propofol (0.3-0.5 mg/kg) and was maintained with an IV infusion of propofol (50 μg/kg/min). Neuromuscular blockade was achieved with IV boluses of rocuronium (0.6 mg/kg for induction and 0.2 mg/kg every 30 minutes for maintenance).

A cuffed tracheal tube with an internal diameter of 7, 8, or 9 mm was used for tracheal intubation, and patients were ventilated with a Dräger Zeus anesthesia machine (Dräger, Lübeck, Germany) in volume-controlled mode with descending flow. Ventilation frequency was set to 12-to-14 breaths/minute, and a tidal volume of 7 mL/kg and a positive end-expiratory pressure of 4 cmH_2O were applied. Mechanical ventilation was initiated with a fraction of inspired oxygen (F_IO_2) of 0.5 that was set to 0.8 after CPB.

Before CPB, the membrane oxygenator was primed with 1,500 mL of lactated Ringer's solution. Heparin was administered at a dose of 300 U/kg, with the anticoagulation time maintained at 300 seconds. Moderate hypothermia was induced routinely (esophageal temperature of 32°C). During CPB, mechanical ventilation was stopped, and the ventilator was disconnected without applying positive airway pressure. Before restoring ventilation, the lungs were inflated 3-to-5 times to a peak airway pressure of 30 cmH_2O to facilitate lung recruitment.

Forced Oscillatory Measurements

Changes in the airway and tissue mechanical properties from CPB and sevoflurane were assessed by measuring the low-frequency forced oscillatory input impedance of the lungs, as detailed previously.[6] Briefly, a T-piece with 2 collapsible segments was attached to the distal tracheal tube, with one end connected to the respirator and the other end to a loudspeaker-in-box system. This apparatus made it possible to switch the patient from the respirator to the forced oscillatory setup during the measurements. These were performed by introducing pseudorandom pressure excitations generated by the loudspeaker into the trachea during short (15 s) apneic pauses introduced into the mechanical ventilation. The forcing signal consisted of 15-integer multiple components of the 0.4-Hz fundamental frequency, between 0.4 and 6 Hz. A 28-mm internal diameter screen pneumotachograph connected to a differential pressure transducer (ICS model 33NA002D; IC Sensors, Milpitas, CA) was used to measure tracheal airflow. An identical pressure transducer was used to detect airway opening pressure. Lung input impedance was computed from the power spectra of airway opening pressure and tracheal airflow and then ensemble-averaged under each condition. The mean lung impedance data were fitted using a well-validated 4-parameter model[19] containing a frequency-independent airway resistance (Raw) and inertance (Iaw) and a constant-phase tissue compartment characterized by the coefficients of

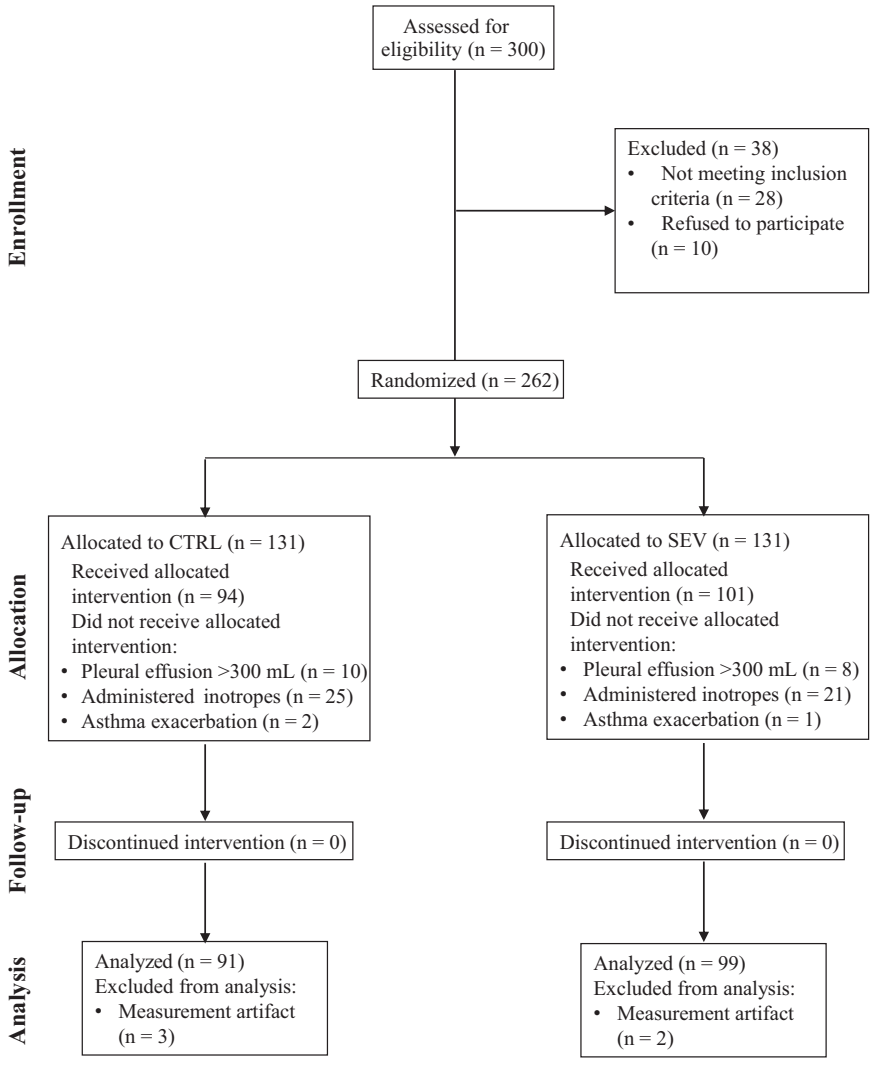

Fig 1. CONSORT flow diagram.

Table 1
Demographic, Anthropometric, and Clinical Characteristics of the Patients

Group	CTRL (n = 91)	SEV (n = 99)
Male/female	54/37	53/46
Age, y	65 ± 14	63 ± 14
Height, cm	167 ± 9	168 ± 10
Weight, kg	79 ± 16	82 ± 16
Surgery		
AVR/AVP	58	58
AVR+CABG	13	8
MVM/MVP	17	21
Other	11	4
Respiratory comorbidities		
Asthma	4	5
Emphysema	9	12

NOTE. Anthropometric data are presented as mean ± standard deviation.
Abbreviations: AVR/AVP, aortic valve replacement/plasty; CABG, coronary artery bypass grafting; MVR/MVP, mitral valve replacement/plasty; Other, left atrial myxoma removal, tricuspid valve plasty, atrial septal defect closure, ascending aorta aneurysm repair.

damping (G) and elastance (H) such that the differences between measured and modeled impedance values were minimal. Lung tissue hysteresivity was calculated as $\eta = G/H$. Raw represents the flow resistance of the bronchial tree, and Iaw is related to the mass of the gas in the airways. The tissue parameters characterize the resistive (G) and elastic properties of the lung parenchyma (H), and η reflects the coupling between the resistive and elastic properties.

Recording and Analyses of the Expiratory Capnogram

Changes in carbon dioxide (CO_2) partial pressure in the exhaled gas during mechanical ventilation were measured with a calibrated mainstream capnograph (Capnogard Model 1265, Novametrix, Andover, MA). The measured signals were digitized at a sampling frequency of 102.4 Hz and stored on a computer.

Custom-made software was used to determine the capnogram parameters. The phase III slope of the time capnogram

(S_{III}) was assessed by fitting a linear regression line to the last 60% of phase III.[20–22] Likewise, the phase II slope (S_{II}) was obtained by fitting a regression line to the points within 20% of time around the inflexion point of phase II.[23]

Analyses of Blood Gas

The partial pressure of oxygen in the arterial blood (PaO_2) was determined from arterial blood gas samples for the PaO_2/F_IO_2 ratio and the arterial-to-end-tidal CO_2 gradient ($P_{a\text{-}ET}CO_2$). The intrapulmonary shunt fraction (Qs/Qt) was determined using the Berggren equation[24]: $Qs/Qt = (CcO_2 - CaO_2)/(CcO_2 - CvO_2)$, where CcO_2, CaO_2, and CvO_2 are the oxygen contents of the pulmonary capillary and arterial and central venous blood, respectively. CcO_2 was calculated according to the alveolar gas equation, assuming the oxygen saturation of hemoglobin in the pulmonary capillaries to be 100%: $CcO_2 = 1.34\ mL/g \times Hb + Sol \times (F_IO_2 \times 713\ mmHg - PaCO_2/0.8)$, where 1.34 mL/g is Hüfner's constant, Hb is the hemoglobin concentration in grams, Sol is 0.0031 mL/100 mL/mmHg, 713 mmHg is the total dry gas pressure, $PaCO_2$ is the partial pressure of CO_2 in the arterial blood, and 0.8 is the respiratory exchange ratio.

Measurement Protocol

The scheme of the experimental protocol is outlined in Figure 2. When stable hemodynamic and respiratory mechanical conditions had been reached after sternotomy, baseline measurements were performed 5 minutes before starting CPB. Measurements included recordings of four 15-second capnogram traces; analyses of arterial and central venous blood gas samples (Radiometer ABL TM 505; Radiometer, Copenhagen, Denmark); registration of the dynamic respiratory compliance displayed by the ventilator (C); and collection of 4 lung input impedance data epochs. The same set of data was gathered 5 minutes after weaning the patient from CPB, when stable circulatory and ventilator conditions were reestablished. Subsequently, in group SEV, 1 age-related minimal alveolar concentration (MAC)[25] of sevoflurane was achieved by setting the vaporizer to 1.4% to 1.9% and the fresh gas flow to 16 L/min, and maintained for 5 minutes with a fresh gas flow of 2 L/min. This interval was chosen based on a previous study, in which respiratory mechanics were found to reach a steady-state condition after administering 1 MAC of sevoflurane for 5 minutes after the peak effect of an allergen provocation in rabbits.[16] Ventilation was maintained without intervention in the patients in group CTRL for a matching period. The third data collection step was taken in the same manner, as detailed earlier in both groups of patients.

Statistical Analyses

Sample size was estimated for a 2-way repeated measures analysis of variance on H as the primary outcome variable with an expected effect size of 0.2 (ie, an approximately 20% change after sevoflurane); a power of 0.8; and 2-sided alpha error of 0.05.[26] The estimation resulted in a required sample size of 97 for each group.

Two-sample *t*-tests were applied to compare mean age, height, and weight between the protocol groups. The chi-square test was used to test the independence of group allocation and sex and the distribution of surgery types within each group.

Scatters in measured variables are expressed as standard error of the mean. The normality of the data was tested using the Kolmogorov-Smirnov test with a Lilliefors correction. Two-way repeated measures analysis of variance with the inclusion of an interaction term was used for all measured variables, with the protocol stage as within-subject factor (before CPB, after CPB, and after intervention) and group allocation as between-subject factor (group SEV or group CTRL) to establish the effects of CPB and the subsequent administration of sevoflurane. The Holm-Sidak multiple comparison procedure was adopted to compare the variables in the study groups at different protocol stages. When comparing 2 samples, the Student *t*-test was used for normality and the Mann-Whitney rank sum test otherwise. The statistical tests were performed with a SigmaPlot statistical software package, Version 13 (Systat, San Jose, CA). All reported p values are 2-sided.

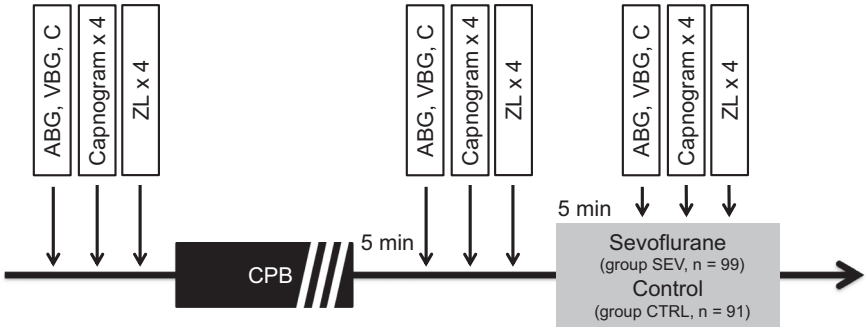

Fig 2. Timeline for the experimental protocol. Measurements were performed with open chest condition at the following 3 stages of cardiac surgery: before starting CPB, 5 minutes after weaning from CPB, and after 5 minutes of intervention (administration of sevoflurane at 1 MAC [group SEV] or unaltered anesthesia management [group CTRL]). At each stage, arterial and central venous blood gas samples were analyzed, the dynamic lung compliance displayed by the ventilator was documented, four 15-second capnogram traces were recorded, and 4 impedance measurements (ZL) were performed.

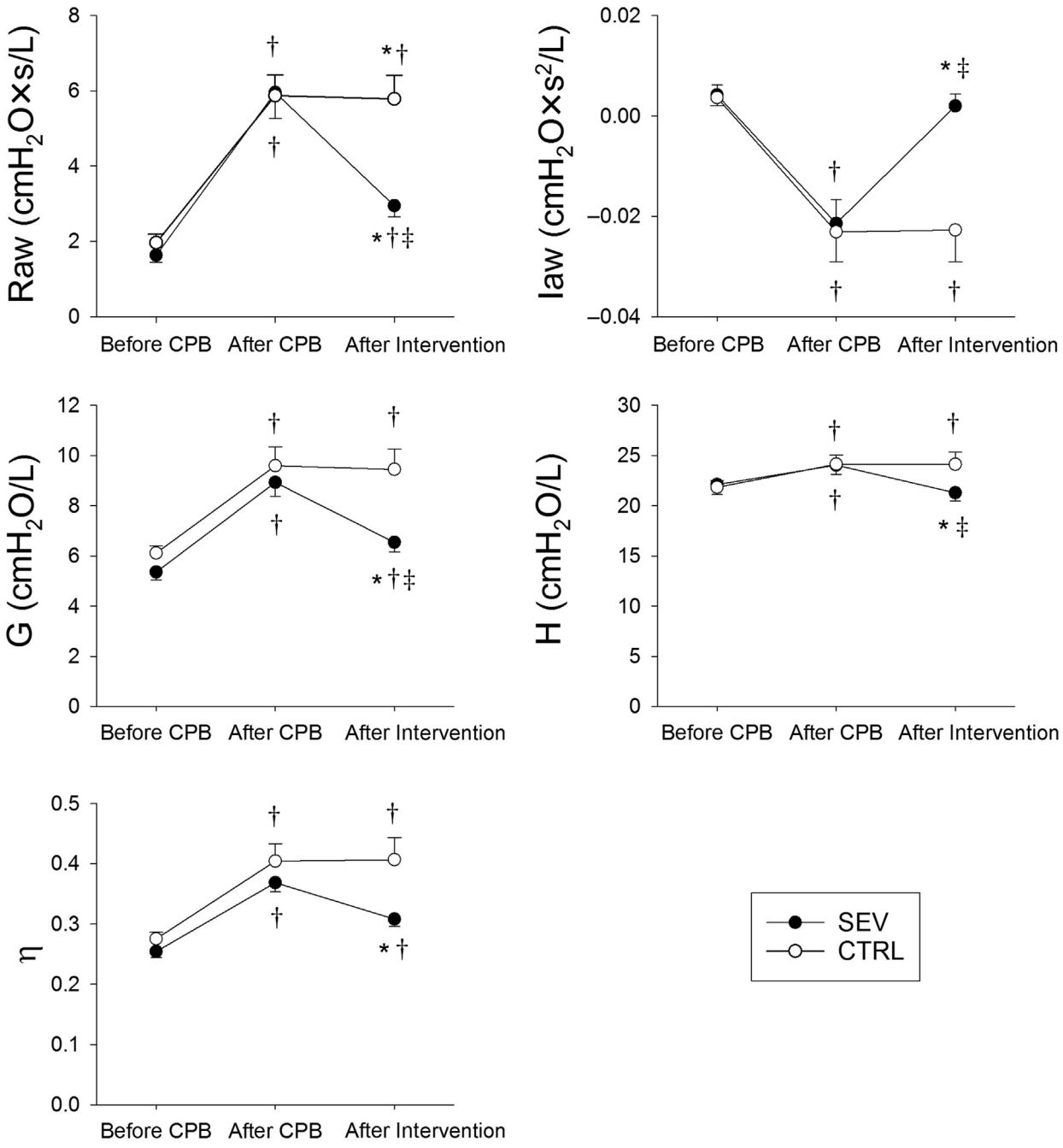

Fig 3. Forced oscillatory airway (Raw: airway resistance; Iaw: airway inertance) and tissue (G: tissue damping; H: tissue elastance; η: tissue hysteresivity) parameters in the group treated with sevoflurane at 1 MAC for 5 minutes (SEV) and the control group with intravenous anesthesia maintained (CTRL). Error bars represent standard error of the mean; *$p < 0.05$ versus condition "after CPB" within a group; †$p < 0.05$ versus condition "before CPB" within a group; ‡$p < 0.05$ between protocol groups within a stage.

Results

No significant difference was found between the protocol groups in age, height, or weight. The distribution of sex, surgery types, and respiratory comorbidities was independent of group allocation (Table 1).

Airway and lung tissue mechanical parameters in both protocol groups at the different stages of the study protocol are demonstrated in Figure 3. The CPB-induced changes in any of the measured parameters in group CTRL were not significantly different from those in group SEV. CPB induced a significant change in all the mechanical parameters, with the most pronounced elevations in Raw (pooled changes of 287% ± 17%), marked decreases in Iaw (–0.025 ± 0.002 $cmH_2O \times s^2/L$), and increases in G (98% ± 27%), whereas rises in H and η were smaller (15% ± 2.3% and 86% ± 32%, respectively; $p < 0.0005$ for all). Sevoflurane induced marked drops in Raw (–43% ± 1.9%, $p < 0.001$); rises in Iaw (–0.024 ± 0.003 $cmH_2O \times s^2/L$); reductions in G (–23% ± 2.9%, $p < 0.001$ for all); and moderate decreases

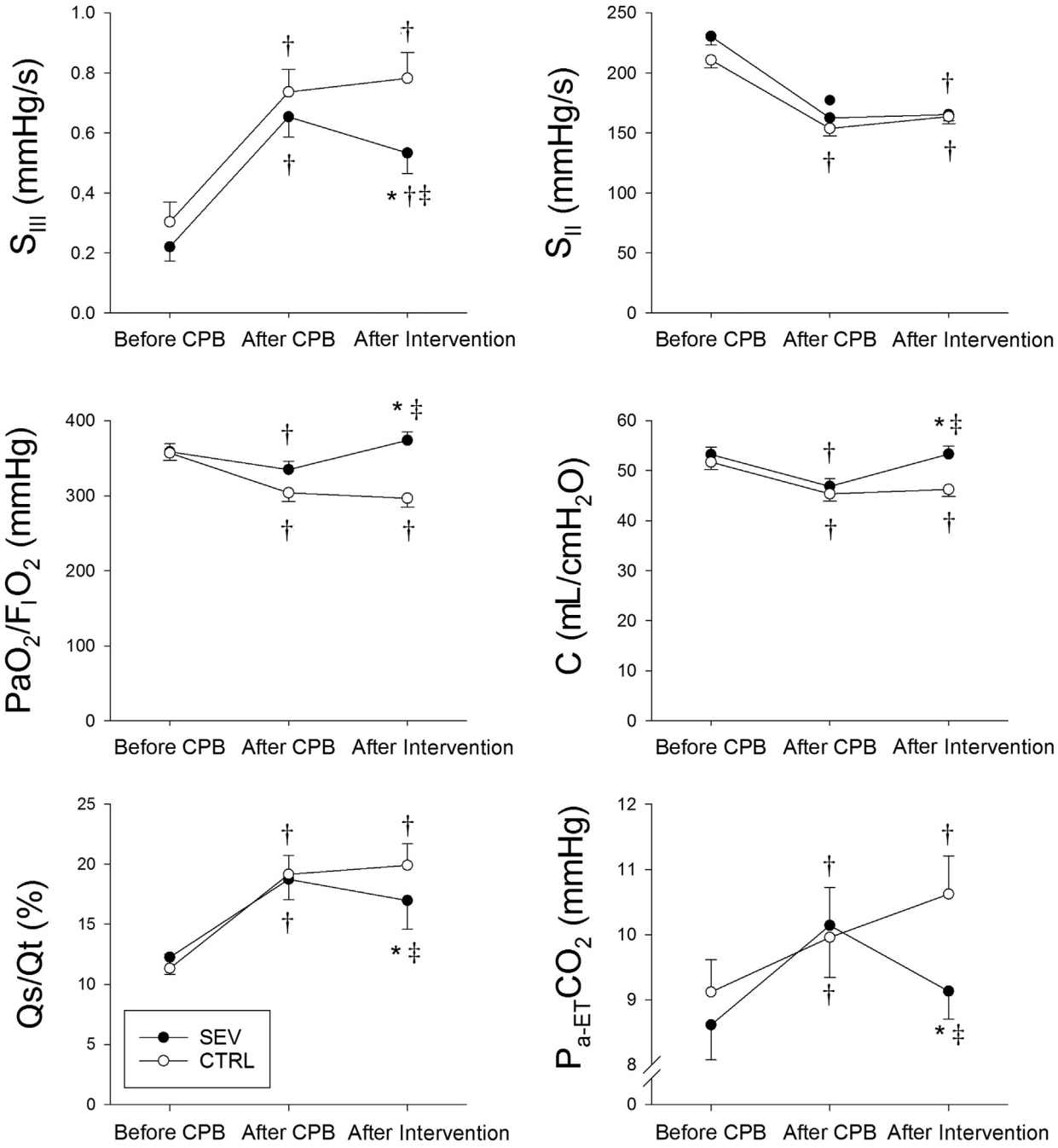

Fig 4. Phase III (S_{III}) and phase II slopes (S_{II}) of time capnograms, lung compliance (C), PaO_2/F_IO_2 ratio, intrapulmonary shunt fraction (Qs/Qt), and arterial-to-end-tidal CO_2 gradient ($P_{a-ET}CO_2$) in the group treated with sevoflurane at 1 MAC for 5 minutes (SEV) and the control group (CTRL). Error bars represent the standard error of the mean; *$p < 0.05$ versus condition "after CPB" within a group; †$p < 0.05$ versus condition "before CPB" within a group; ‡$p < 0.05$ between protocol groups within a stage.

in H (–10% ± 2.0%, $p < 0.001$) and η (9.0% ± 4.0%, $p < 0.02$). There was no evidence of a statistically significant detectable change in any of the parameters in the corresponding time-matched changes in group CTRL.

Capnogram phase slopes, lung compliance, and parameters associated with oxygenation are demonstrated in Fig 4. The phase III slope of the capnogram exhibited markedly significant increases after CPB in both protocol groups, with pooled changes of 0.46 ± 0.04 mmHg/s ($p < 0.0001$). After application of sevoflurane, S_{III} decreased (–0.15 ± 0.036 mmHg/s, $p < 0.02$), whereas it did not change significantly in group CTRL. No significant difference was found in S_{II} between the protocol groups at any stage ($p > 0.13$). The phase II slope decreased markedly after CPB (28% ± 1.5%, $p < 0.0001$) and increased slightly at the last stage in both groups (9.8% ± 1.8%, $p < 0.02$). The changes in the PaO_2/F_IO_2 ratio, C, Qs/Qt, and $P_{a-ET}CO_2$ subsequent to CPB did not differ significantly between the protocol groups. The PaO_2/F_IO_2 ratio and C exhibited significant decreases after CPB (pooled changes of –9.3% ± 2.1% and –13% ± 1.0%,

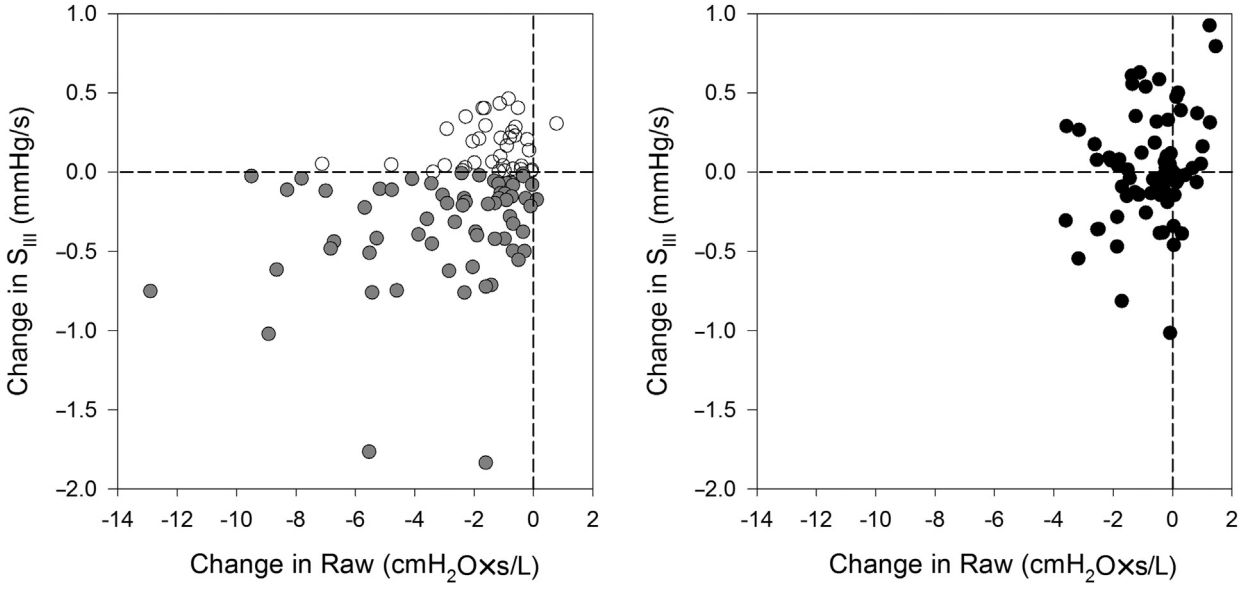

Fig 5. Association between changes in airway resistance and phase III slope (S_{III}) after administration of sevoflurane at 1 MAC for 5 minutes (group SEV, *left*) or IV anesthesia was maintained (group CTRL, *right*) in each patient. In the left panel, *empty symbols* represent patients with increasing S_{III}, whereas *filled symbols* represent patients with decreasing S_{III} from sevoflurane.

respectively), whereas Qs/Qt and $P_{a\text{-}ET}CO_2$ increased (119% ± 9% and 32% ± 9%, respectively; $p < 0.0001$ for all). Sevoflurane reversed the decreases in the PaO_2/F_IO_2 ratio and C (15% ± 1.7% and 17% ± 1.4%, respectively; $p < 0.0001$ for both) and reduced Qs/Qt and $P_{a\text{-}ET}CO_2$ (−20% ± 1.5% and −9.7% ± 3.3%, respectively; $p < 0.03$). The corresponding changes in the PaO_2/F_IO_2 ratio, C, and Qs/Qt in group CTRL were not significant.

Figure 5 depicts the associations between the changes in Raw and S_{III} after the interventions. Sevoflurane decreased Raw in all but 1 patient, whereas the changes in S_{III} were far less uniform; the administration of sevoflurane resulted in further elevations in S_{III} in 36 of 99 patients. In contrast, 28 of the 91 patients in group CTRL exhibited additional elevations in Raw during the corresponding period, and S_{III} increased in 35 patients.

The association of post-CPB values of the PaO_2/F_IO_2 ratio and $P_{a\text{-}ET}CO_2$ and their sevoflurane-induced changes are demonstrated in Figure 6. No statistically significant correlation was observed between the PaO_2/F_IO_2 ratio and its change after sevoflurane ($R^2 = 0.05$), whereas a strong negative correlation was found between $P_{a\text{-}ET}CO_2$ and its change after sevoflurane ($R^2 = 0.51$, $p < 0.001$).

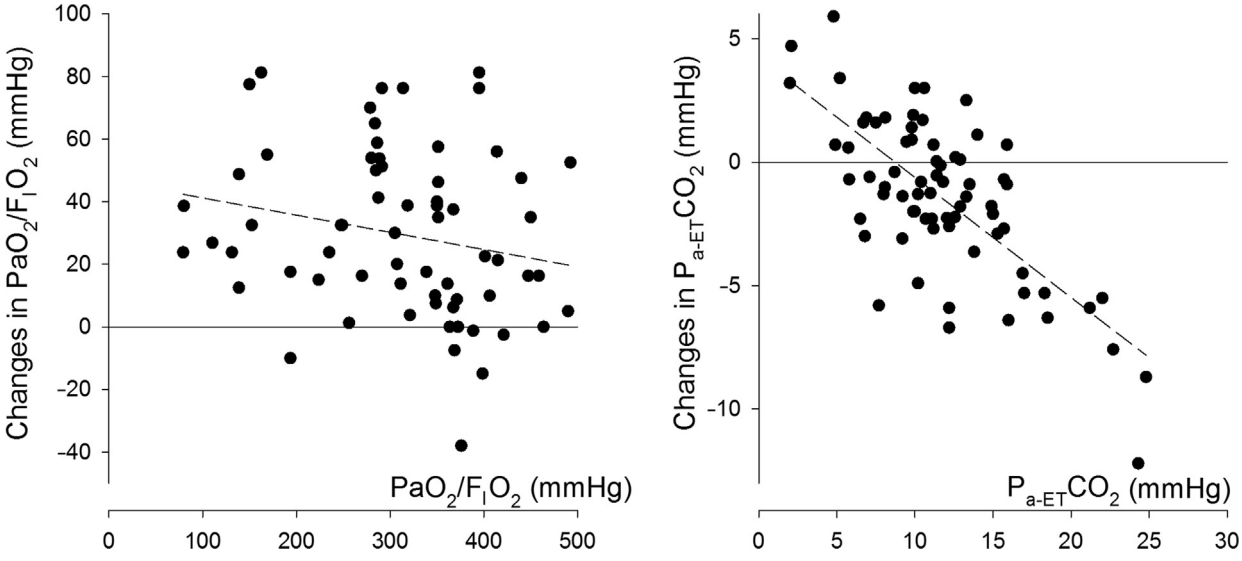

Fig 6. Association between post-CPB values of the PaO_2/F_IO_2 ratio (left) and $P_{a\text{-}ET}CO_2$ (right) and their sevoflurane-induced changes. Each *symbol* represents a patient; *dashed lines* denote linear regressions.

Discussion

The results of this study demonstrated the ability of sevoflurane to reverse detrimental changes in lung function induced by extracorporeal circulation in a large cohort of cardiac surgery patients. Administration of sevoflurane uniformly led to marked airway dilations in almost all the patients, resulting in improved function of the lung as an oxygenator. Conversely, this beneficial profile of sevoflurane was reflected in distinctly different changes in the capnogram parameter related to ventilation heterogeneities (S_{III}). Even though the parameters presented improved unanimously after the administration of sevoflurane, none of them showed significant changes in group CTRL during the matching period.

Airway and Lung Tissue Mechanics

Sevoflurane induced significant improvements in the airway and tissue mechanics compromised by CPB. This finding was in accordance with previous results, in which the beneficial profile of sevoflurane was demonstrated against bronchoconstriction induced by exogenous cholinergic agonists[1,2] or after a release of endogenous mediators.[3] Because Raw mainly reflects the flow resistance of the central conducting airways,[27] the marked drops in this parameter likely were a reflection of the prominent dilation of proximal airway regions. This idea was supported by the complete return of Iaw to pre-CPB levels in group SEV, which may have resulted from the rise of bronchial volume as a consequence of bronchodilation[27] and from the homogenization of airway calibers.[28] The drops in lung tissue parameters G and H after the administration of sevoflurane may reflect an improvement in the parenchymal viscoelasticity because sevoflurane was reported to have pulmonary anti-inflammatory effects.[29,30] However, such a process was not likely to evolve due to the relatively short time frame (5 min). Another, more probable, mechanism responsible for the improvement in tissue parameters may be due to alveolar recruitment secondary to bronchodilation and homogenization of alveolar ventilation. Accordingly, the drops in G can be explained by decreasing time constant inequalities arising from the heterogenous constriction of small airways. Because sevoflurane induced greater drops in G than in H, their ratio η decreased after the administration of sevoflurane, supporting the notion of lung homogenization.[31] The improved lung aeration from sevoflurane also was supported by the increases in a routinely assessed mechanical parameter reflecting overall lung tissue stiffness (C).

Ventilation and Oxygenation

The phase III slope of the capnogram is determined by the ventilation and perfusion of the lungs, although the latter process only accounts for ~20% of the change in S_{III}.[32] Furthermore, the slope of CO_2 concentration during alveolar emptying is governed primarily by Raw.[23] Accordingly, an increment in S_{III} mainly reflects the maldistribution of ventilation, as observed in asthma,[33] in obstructive lung disease,[21] or after CPB,[23] whereas bronchodilator therapy[34] or an optimized ventilation strategy[20,22,35] decreases S_{III}. Considering these earlier findings, the decrement in the mean S_{III} in the study presented here implied the reduction of ventilation heterogeneity from sevoflurane. This result was in accordance with the beneficial lung mechanical changes, as previously described.

The lack of difference in the change in S_{II} between the protocol groups can be explained by the dependence of this parameter on various lung mechanical properties. In a previous study, the change in S_{II} exhibited a negative correlation with the change in Raw and a positive correlation with the change in C.[23] Because sevoflurane induced changes in both of these mechanical parameters, their effects on S_{II} may have been counterbalanced.

The improvement of ventilation from sevoflurane was manifested in better ventilation-perfusion matching as reflected by the decreased Qs/Qt and a related, more easily accessible parameter, $P_{a\text{-}ET}CO_2$. Several studies have investigated the effect of sevoflurane on the intrapulmonary shunt fraction, but they were focused on the potential inhibition of hypoxic pulmonary vasoconstriction by this volatile agent during one-lung ventilation. Abe et al reported a decrease in Qs/Qt after switching from sevoflurane to propofol,[36] whereas Beck et al observed similar changes in Qs/Qt among patients receiving either sevoflurane or propofol.[37] The discrepancies in these findings can be attributed to the dual action of sevoflurane; although it inhibits hypoxic pulmonary vasoconstriction via vascular smooth muscle relaxation, it also decreases ventilation-perfusion mismatch by facilitating a more uniformly distributed ventilation. In the study presented here, the striking bronchodilation from sevoflurane opened shunted alveolar regions with sustained perfusion in both lungs. The resultant improvement in ventilation-perfusion matching most likely outweighed the potential loss of protective hypoxic pulmonary vasoconstriction, as reflected in the decreased Qs/Qt and $P_{a\text{-}ET}CO_2$. These beneficial changes ultimately resulted in better oxygenation, as reflected by the increased PaO_2/F_IO_2 ratio. A further noteworthy observation is that the higher the $P_{a\text{-}ET}CO_2$ after CPB, the greater its improvement with sevoflurane. Even though this relationship is less apparent for the absolute changes in PaO_2/F_IO_2, this is of greater importance in patients with low PaO_2/F_IO_2 after CPB. These findings indicated the particular benefit of sevoflurane in patients with severely compromised gas exchange.

Effect of Sevoflurane on Ventilation Heterogeneity

Despite the association between airway caliber and S_{III},[23] the magnitude of the decrement in S_{III} after the administration of sevoflurane did not match that in Raw. Thus, the authors sought to elucidate the origin of this discrepancy by investigating the association between the changes in Raw and in S_{III} after the post-CPB intervention in both protocol groups. Whereas Raw decreased spontaneously in about two-thirds of the patients in group CTRL after CPB, bronchodilation was observed in all the patients but 1 in group SEV. Despite this uniform change in Raw in the latter group, S_{III} exhibited

diverse changes, with further elevations in more than one-third of the patients. This suggested that in these patients, airway dilation resulted in a more heterogenous alveolar emptying.

Limitations and Future Directions

Because the low-frequency forced oscillation technique requires general anesthesia and mechanical ventilation, this study was limited to the assessment of intraoperative changes in pulmonary mechanics, ventilation, and oxygenation. Systematic evaluation of the duration of the pulmonary effects of sevoflurane and its possible postoperative benefits (eg, shorter extubation time and intensive care unit stay, lower frequency and severity of respiratory morbidities) may be a subject of a future investigation. Additional research may focus on the characterization of the preventive potential of sevoflurane administered into the oxygenator during CPB in patients with airway susceptibilities. Another possible direction for forthcoming research is the investigation of the potential respiratory benefit of sevoflurane in intensive care unit patients with respiratory complications, in whom its administration can be achieved by using the anesthetic-conserving device (AnaConDa; Sendana Medical, Kildare, Ireland).

In conclusion, the results of the present study demonstrated that bronchoconstriction with subsequent development of atelectasis and intrapulmonary shunt triggered by CPB can be alleviated effectively with the application of sevoflurane. This benefit may be of particular importance in patients with airway hyper-responsiveness, in whom severe bronchoconstriction is likely to develop after CPB. In such patients, switching anesthesia management from a total intravenous approach to an inhalation technique may be recommended. The potential increase in ventilation heterogeneity after sevoflurane may necessitate the elevation of positive end-expiratory pressure and/or applying recruitment maneuvers.

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